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[57] —SA **ABSTRACT**

This invention is directed to novel substituted nucleotide bases with a crosslinking arm which accomplish crosslinking between specific sites on adjoining strands of oligonucleotides or oligodeoxynucleotides. The invention is also directed to oligonucleotides comprising at least one of these crosslinking agents and to the use of the resulting novel oligonucleotides for diagnostic and therapeutic purposes. The crosslinking agents of the invention are of the following formula (I):

$$R_1—B—(CH_2)_q—(Y)_r—(CH_2)_m—A' \quad (I)$$

wherein,

R_1 is hydrogen, or a sugar moiety or analog thereof optionally substituted at its 3' or its 5' position with a phosphorus derivative attached to the sugar moiety by an oxygen and including groups Q_1 Q_2 and Q_3or with a reactive precursor thereof suitable for nucleotide bond formation;

Q_1 is hydroxy, phosphate or diphosphate;

Q_2 is =O or =S;

Q_3 is CH_2—R', S—R', O—R', or N—R'R";

each of R' and R" is independently hydrogen or C_{1-6} alkyl;

B is a nucleic acid base or analog thereof that is a component of an oligonucleotide;

Y is a functional linking group;

each of m and q is independently 0 to 8, inclusive;

r is 0 or 1; and

A' is a leaving group.

This invention is also directed to novel 3,4-disubstituted and 3,4,-trisubstituted pyrazolo[3,4-d]-pyrimidines and to the use of these nucleic acid bases in the preparation of oligonucleotides. The invention includes nucleosides and mono- and oligonucleotides comprising at least one of these pyrazolopyrimidines, and to the use of the resulting novel oligonucleotides for diagnostic purposes. EA

15 Claims, 3 Drawing Sheets